David M. Hilbert, Ph.D.

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Summary

Over the past 11 years, I have combined my disciplined approach to science with the business of effective drug development and corporate management. The expertise gained has afforded me a unique appreciation of the biotech environment and the experience to transform the many challenges within that environment into opportunities for success. Currently, I am an independent biotech consultant with several clients in the Maryland biotech corridor. Previously, I was a member of the senior management team at Cellective Therapeutics, a start-up antibody company acquired by MedImmune in October 2005. Prior to Cellective, I was Vice President, Research at Human Genome Sciences. The Research group consisted of 104 dedicated scientists, research associates and support personnel responsible for discovery, target validation, antibody development, assay development, toxicology, pharmacokinetics, clinical testing and animal husbandry functions. Prior to HGS, I was a Staff Fellow in the National Cancer Institute, NIH.

Experience

2005 – Date Independent Consultant

- Consulted for MedImmune in the transition and integration of Cellective antibody programs
- Consulted for two additional companies on strategic direction and drug development programs

2004 – 2005 Vice President, Research Cellective Therapeutics, Inc. Gaithersburg, MD

- Participated in raising Series A financing of \$27.5 million
- Member of the executive management team consisting of the CEO, VP Business Development, and the VP Research.
- Worked with Cellective investor base to enhance company value through timely product development, strategic partnership(s) and effective contract negotiations

- Coordinated filing of patents with outside legal counsel
- Established and managed strategic CRO alliances to provide manufacturing, preclinical, regulatory and clinical support
- Outsourced and managed mAb manufacturing
- Developed exit strategies that ultimately led to the acquisition of company by MedImmune in late 2005

1996 – 2004 Vice President, Research, Human Genome Sciences, Inc.

- Utilized genomics-based drug discovery platforms to identify secreted proteins with therapeutic and diagnostic potential
- Developed *in vitro* and *in vivo* high throughput biological screening assays for target identification and validation
- Identified B Lymphocyte Stimulator (BLyS) and its role in normal B cell development and autoimmune disease
- Developed radioconjugate of BLyS (LymphoRad) for the treatment of neoplastic B cell disease
- Identified role of Ck-beta-9 in immune cell mobility and function
- Developed therapeutic mAb directed against BLyS for the treatment of autoimmune diseases
- Investigated mechanism(s) of action of IL6 and BLyS in B lymphocytes
- Recruited leading clinicians in the fields of autoimmunity and oncology to serve on Clinical Advisory Boards.
- Directed preclinical development (pharmacology, efficacy, safety, toxicology, pharmacokinetics, and dose and route rationale) to support IND filings
- Co-developed multiple Phase 1 and Phase 2 clinical programs for BLyS, LymphoRad, and LymphoStat (anti-BLyS mAb)
- Created clinical testing department at HGS responsible for the development, validation, and execution of all clinical sample tracking, testing, analyses and reporting protocols. Developed systems for automated data collection, quality assessment and transfer of results to the appropriate clinical trials databases.
- Outsourced and managed contract manufacturing of LymphoRad (radiolabeled BLyS) for research and clinical use
- Established and directed numerous expert advisory panels for scientific and clinical development

- Collaborated with Marketing and Business Development to create target drug profiles for compounds emerging from the Research Department
- Coalesced three independent research groups into a unified HGS Research
 Department. The newly formed department consisted of 104 dedicated employees
 who collectively were responsible for the company's research, antibody
 development, assay development, toxicology, pharmacokinetics, clinical testing
 and animal husbandry functions.
- Standing member of the HGS Product Development Committee comprising the heads of Research, Regulatory, Clinical, Project Management, Business Development, and Manufacturing. Team was responsible for defining and executing appropriate corporate strategies for each drug candidate.
- Developed and implemented performance-based employee bonus programs

Education

- 1979 B.S. Biology, Haverford College, Haverford, PA
- 1987 Ph.D. Immunology, University of Pennsylvania, Philadelphia, PA

Publications

Cancro, M. P., M. A. Thompson, and D. M. Hilbert. 1983. Developmental aspects of B-cell repertoire phenotype. *Surv. Immunol. Res.* 2:62.

Hilbert, D. M. and M. P. Cancro. 1986. A comparative analysis of the anti-phosphorylcholine response of CLA and BALB/c mice. *Curr. Top. Microbiol. Immunol.* 127:206.

Hilbert, D. M. and M. P. Cancro. 1988. Characterization of an inbred mouse exhibiting low responsiveness to phosphorylcholine. Antibodies from low-responder mice suggest gene conversion events within the S107VH gene family. *J. Immunol.* 140:4364.

Hilbert, D. M., M. P. Cancro, P. A. Scherle, R. P. Nordan, J. Van Snick, W. Gerhard, and S. Rudikoff. 1989. T cell derived IL-6 is differentially required for antigen-specific antibody secretion by primary and secondary B cells. *J. Immunol.* 143:4019.

Degrassi, A., D. M. Hilbert, A. O. Anderson, M. Potter, and H. G. Coon. 1990. In vitro culture of a primary plasmacytoma that has retained its dependence on pristane conditioned microenvironment for growth. *Curr. Top. Microbiol. Immunol.* 166:71.

- Degrassi, A., D. M. Hilbert, S. Rudikoff, A. O. Anderson, M. Potter, and H. G. Coon. 1993. In vitro culture of primary plasmacytomas requires stromal cell feeder layers. *Proc. Natl. Acad. Sci. U. S. A.* 90:2060.
- Hilbert, D. M., J. G. Pumphrey, J. Troppmair, U. R. Rapp, and S. Rudikoff. 1993. Susceptibility and resistance to J3V1 retrovirus-induced murine plasmacytomagenesis in reconstituted severe combined immunodeficient mice. *Oncogene*. 8:1993.
- Hilbert, D. M., K. L. Holmes, A. O. Anderson, and S. Rudikoff. 1993. Long-term thymic reconstitution by peripheral CD4 and CD8 single- positive lymphocytes. *Eur. J. Immunol.* 23:2412.
- Shaughnessy, J. D., Jr., J. D. Owens, Jr., F. Wiener, D. M. Hilbert, K. Huppi, M. Potter, and J. F. Mushinski. 1993. Retroviral enhancer insertion 5' of c-myc in two translocationnegative mouse plasmacytomas upregulates c-myc expression to different extents. *Oncogene*. 8:3111.
- Degrassi, A., A. De Maria, G. Lisignoli, N. Zini, P. Sabatelli, L. Cirillo, M. C. Monaco, D. M. Hilbert, F. S. Ambesi-Impiombato, and N. M. Maraldi. 1994. Transfer of HIV-1 to human tonsillar stromal cells following cocultivation with infected lymphocytes. *AIDS Res. Hum. Retroviruses.* 10:675.
- Hilbert, D. M., A. O. Anderson, K. L. Holmes, and S. Rudikoff. 1994. Long-term lymphoid reconstitution of SCID mice suggests self-renewing B and T cell populations in peripheral and mucosal tissues. *Transplantation*. 58:466.
- Nazarov, V., D. Hilbert, and L. Wolff. 1994. Susceptibility and resistance to Moloney murine leukemia virus-induced promonocytic leukemia. *Virology*. 205:479.
- Hilbert, D. M., M. Y. Shen, U. R. Rapp, and S. Rudikoff. 1995. T cells induce terminal differentiation of transformed B cells to mature plasma cell tumors. *Proc. Natl. Acad. Sci. U. S. A.* 92:649.
- Fernandez-Salguero, P., T. Pineau, D. M. Hilbert, T. McPhail, S. S. Lee, S. Kimura, D. W. Nebert, S. Rudikoff, J. M. Ward, and F. J. Gonzalez. 1995. Immune system impairment and hepatic fibrosis in mice lacking the dioxin-binding Ah receptor [see comments]. *Science* 268:722.
- Hilbert, D. M., M. Kopf, B. A. Mock, G. Kohler, and S. Rudikoff. 1995. Interleukin 6 is essential for in vivo development of B lineage neoplasms. *J. Exp. Med.* 182:243.
- Lisignoli, G., M. C. Monaco, A. Facchini, S. Toneguzzi, L. Cattini, D. M. Hilbert, S. Lavaroni, O. Belvedere, and A. Degrassi. 1996. In vitro cultured stromal cells from

human tonsils display a distinct phenotype and induce B cell adhesion and proliferation. *Eur. J. Immunol.* 26:17.

Hilbert, D. M., T. S. Migone, M. Kopf, W. J. Leonard, and S. Rudikoff. 1996. Distinct tumorigenic potential of abl and raf in B cell neoplasia: abl activates the IL-6 signaling pathway. *Immunity*. 5:81.

Romanova, L. Y., I. A. Alexandrov, G. Schwab, D. M. Hilbert, J. F. Mushinski, and R. P. Nordan. 1996. Mechanism of apoptosis suppression by phorbol ester in IL-6-starved murine plasmacytomas: role of PKC modulation and cell cycle. *Biochemistry* 35:9900.

*Fernandez-Salguero, P. M., D. M. Hilbert, S. Rudikoff, J. M. Ward, and F. J. Gonzalez. 1996. Aryl-hydrocarbon receptor-deficient mice are resistant to 2,3,7,8-tetrachlorodibenzo-p-dioxin-induced toxicity. *Toxicol. Appl. Pharmacol.* 140:173.

Roschke, V., P. Hausner, E. Kopantzev, J. G. Pumphrey, M. Riminucci, D. M. Hilbert, and S. Rudikoff. 1998. Disseminated growth of murine plasmacytoma: similarities to multiple myeloma *Cancer Res.* 58:535.

Hilbert, D. M., Theisen, P. W., Rudikoff, E. K., and S. R. Bauer, 1998. Interaction of abl and raf with IL-7 signaling pathway and transformation pf pre-B cells from resistant mice. *Oncogene* 17:2125.

Belvedere, O., Feruglio, C., Malangone, W., Bonora, M. L., Donini, A., Dorotea, L., Tonutti, E., Rinaldi, C., Pittini, M., Baccarani, M., Del Frate, G., Biffoni, F., Sala, P., Hilbert, D. M., and Degrassi, A. 1999. Phenotypic characterization of immunomagnetically purified umbilical cord blood CD34+ cells. *Blood Cells, Molecules, and Disease*. 25:141-146.

Belvedere, O., Feruglio, C., Malangone, W., Bonora, M. L., Minisini, A. M., Spizzo, R., Donini, A., Sala, P., De Anna, D., Hilbert, D. M., and Degrassi, A. 2000. Increased blood volume and CD34+CD38- progenitor cell recovery using a novel umbilical cored blood collection system. *Stem Cells* 18:245.

Gronowski, A. M., Hilbert, D. M., Sheehan, K. C., Garotta, G., Schreiber, R. D. 1999. Baculovirus stimulates antiviral effects in mammalian cells. *J Virol*. 73:9944-51.

Moore, P.A., Belvedere, O., Orr, A., Pieri, K., LaFleur, D.W, Feng, P., Soppet, D., Charters, M., Gentz, R., Parmelee, D., Li, Y., Galperina, O., Giri, J., Roschke, V., Nardelli, B., Carrell, J., Sosnovtseva, S., Greenfield, W., Ruben, S. M., Olsen, H. S., Fikes, J., Hilbert, D. M. 1999. BLyS: member of the tumor necrosis factor family and B lymphocyte stimulator. *Science*. 285:260-263.

- Nardelli, B., Belvedere, O., Roschke, V., Moore, P. A., Olsen, H. S., Migone, T. S., Sosnovtseva, S., Carrell, J. A., Feng, P., Giri, J. G., and Hilbert, D. M. 2001. Synthesis and Release of B Lymphocyte Stimulator from Myeloid Cells. *Blood* 97(1):198-204.
- Do, R. K., Hatada, E., Lee, H., Tourigny, M. R., Hilbert, D., Chen-Kiang, S. 2000 Attenuation of apoptosis underlies BLyS enhancement of humoral immune response. *J. Exp. Med.* 192(7):953-964.
- Kanakaraj, P., Migone, T. S., Nardelli, B., Ullrich, S., Li, Y., Olsen, H. S., Salcedo, T. W., Kaufman, T., Chochrane, E., Gan, Y., Hilbert, D. M., Giri, J. 2000. BLyS binds to B cells with high affinity and induces activation of the transcription factors Nf-kB and ELF-1. *Cytokine* 13(1):25-31.
- Cheema, G. S., Roschke, V., Hilbert, D. M., and Stohl, W. 2001, Elevated serum B Lymphocyte Stimulator (BLyS) levels in patients with systemic immune-based rheumatologic diseases. *Arthritis and Rheumatology* 44(6):1313-9.
- Harless, S. M., Lentz, V. M., Sah, A.P., Hsu, B. L., Clise-Dwyer, K, Hilbert' D. M., Hayes, C. E., and Cancro, M.P. 2001. Competition for BLyS-mediated signaling through Bcmd/Br3 regulates peripheral B lymphocyte numbers. *Current Biology*. 11:1986-89.
- Briones, J., Timmerman, J. M., Hilbert, D. M., Levy, R. 2002. BLyS and BLyS receptor expression in non-Hodgkin's lymphoma. *Exp. Hematology* 30:135-141.
- Hsu, B. L., Harless, S. M., Coleman Lindsley, R., Hilbert, D. M., Cancro, M. P. BLyS enables survival of transitional and mature B cells through distinct mediators. *J. Immunol.* 168:5993-96.
- Litinskiy MB, Nardelli B, Hilbert DM, He B, Schaffer A, Casali P, Cerutti A. 2002. DCs induce CD40-independent immunoglobulin class switching through BLyS and APRIL. *Nature Immunol.* 3:822-9.
- Cheema, G. S., Roschke, V., Sosnovtseva, S., Hilbert, D. M., Stohl, W. 2002. Enhancement of circulating levels of autoantibodies by B Lymphocyte Stimulator Protein requires helper T cells: Lessons form HIV-infected patients. *Clin Immunol*. 104:115.
- Roschke, V., Sosnovteseva, S., Ward, C. D., Hong, J. S., Smith, R., Albert, V., Stohl, W., Baker, K., Ullich, S., Nardelli, B., Hilbert, D. M., Migone, T. 2002, BLyS and April form biologically active heterotrimers that are expressed in patients with systemic immune-based rheumatic diseases. *J. Immunol.* 169:4314-4321.
- Nardelli, B., Moore, P. M., Li, Y., and Hilbert, D. M. 2002. BLyS: A therapeutic trichotomy for the treatment of B cell disease. *Leukemia and Lymphoma* 43:1367-1373.

- Tan, S., Roschke, V., Perry,, J. W., Arkfeld, D. G., Ehresmann, G. R., Migone, T., Hilbert, D. M., Stohl, W. 2003. Local production of B Lymphocyte Stimulator (BLyS) protein and A Proliferation-Inducing Ligand (APRIL) in arthritic joints of patients with inflammatory arthritis. *Arthritis and Rheumatology* 48:982-992
- Stewart, D. M., Patel;, D. D., AcAvoy, M., Louie, A., Orr, A., Hong, J., Pieri, K., Heater, M. D., Butscher, A. L., Hilbert, D. M., Buckley, R. H., and Nelson, D. L. 2001, B lymphocytes from patients with Common Variable Immune Deficiency proliferate and secrete Ig in response to B Lymphocyte Stimulator (BLyS). *Clinical Immunology* in press.
- Baker, K. P., Edwards, B. M., Main, S. H., Choi, G., Wager, R. E, Abramian, D., Sekut, L., Sturm, B., Minter, R., Dobson, C. L., Williams, E., Carmen, S., Smith, R., Roschke, V., Ruben, S., Hilbert, D. M., Vaughan, T. J., and Albert, V. R. 2003 Generation and Characterization of LymphoStat-BTM, a Human Monoclonal Antibody that Antagonizes BLyS Bioactivities. *Arthirtis and Rheumatology* in press.
- Stohl W., Metyas S, Tan S.M., Cheema G.S., Oamar B., Xu D., Roschke V., Wu Y., Baker K.P., Hilbert D.M. 2003. B lymphocyte stimulator overexpression in patients with systemic lupus erythematosus: longitudinal observations. Arthritis Rheum. 48(12):3475-86.
- Stohl W., Metyas S., Tan S.M., Cheema G.S., Oamar B., Roschke V., Wu Y., Baker K.P., Hilbert D.M. 2004. Inverse association between circulating APRIL levels and serological and clinical disease activity in patients with systemic lupus erythematosus. Ann Rheum Dis. 63(9):1096-103.
- Fleming T.J., Sachdeva M., Delic M., Beltzer J., Wescott C.R., Devlin M., Lander R.C., Nixon A.E., Roschke V., Hilbert D.M., Sexton D.J. 2005. Discovery of high-affinity peptide binders to BLyS by phage display. J Mol Recognition 18(1):94-102.
- Schaller M., Stohl W., Tan S.M., Benoit V.M., Hilbert D.M., Ditzel H.J. 2005. Raised levels of anti-glucose-6-phosphate isomerase IgG in serum and synovial fluid from patients with inflammatory arthritis Ann Rheum Dis. 64(5):743-9.
- Collins C.E., Gavin A.L., Migone T.S., Hilbert D.M., Nemazee D, Stohl W. 2005. B lymphocyte stimulator (BLyS) isoforms in systemic lupus erythematosus: disease activity correlates better with blood leukocyte BLyS mRNA levels than with plasma BLyS protein levels. Arthritis Res Ther. 2005 Nov 15;8(1):R6.
- Woodland, RT, Hammerman P.S., Schmidt, M.P., Fox, C.J., Opferman, J.T., Korsmeyer, S.J., Hilbert, D. M., Thompson, C.B. 2006. Molecular Basis for B Lymphocyte Stimulator (BLyS)-Dependent B Cell Survival. *Submitted fir publication*.